GEIS Respiratory Disease Surveillance Newsletter

DoD Center for Deployment Health Research
Naval Health Research Center, San Diego

Issue 4 **August 2001**

Sponsored by the DoD Global Emerging Infections System (GEIS), the Naval Health Research Center (NHRC) collaborates with numerous federal and non-federal institutions to conduct surveillance for several respiratory pathogens, including adenovirus, influenza, respiratory syncytial virus (RSV), parainfluenza, *Streptococcus pyogenes*, and invasive *Streptococcus pneumoniae*. Please visit our website at http://www.nhrc.navy.mil/geis for additional information.

Current Study Updates

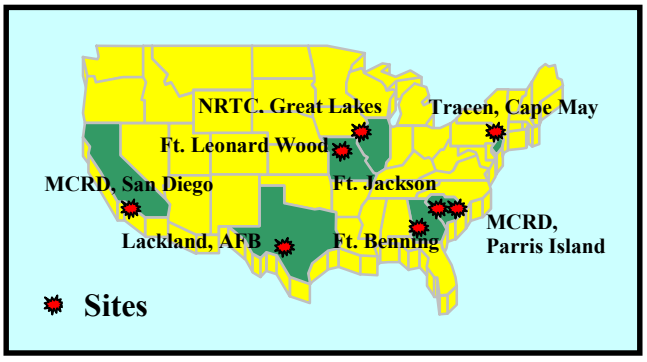
Pneumococcal Study

In collaboration with Centers for Disease Control and Prevention, the Mayo Clinic and Foundation, and Wyeth-Lederle vaccines, NHRC and 4 recruit training sites will conduct a double blind, placebo-controlled trial of a 23-valent pneumococcal vaccine to assess the vaccine's clinical effectiveness among the military trainee population. The study is currently underway at Fort Jackson, Fort Leonard Wood, NRTC, Great Lakes, and most recently, MCRD Parris Island. The study will enroll over 191,000 trainees. The participants will be actively followed during recruit training for pneumonia and passively followed (by tracking inpatient and outpatient military medical databases) after recruit training until the end of the study period (up to 2 years) for pneumonia and acute respiratory disease. To date, study site personnel have enrolled more than 34,000 recruits with a better than 69% enrollment rate.

ZymeTx Rapid Flu Diagnostic

A clinical trial of two rapid tests (ZymteTx, ZstatFlu™ and Quidel, QuickVue®) for influenza will resume enrollment in October 2001. Enrollment for this clinical trial began February 2001 but was postponed in March due to the low levels of patients presenting with FRI symptoms at the two enrollment sites (Ambulatory Care Center, Point Loma, CA and Naval Medical Center, San Diego). To ensure that at least 300 subjects are enrolled, additional enrollment sites may be added.

Febrile Respiratory Illness (FRI) Surveillance



Current Progress – Febrile Respiratory Illness (FRI) surveillance is currently being conducted at eight military training sites. Specimens from trainees presenting with symptoms matching the definition of FRI are tested for adenovirus, influenza A and B, respiratory syncytial virus (RSV), and parainfluenza 1, 2 and 3. The specific trends observed for each of these viruses are described in the following sections.

Geographic Trends – Since January 1, 2001, five of the eight surveillance sites have reported FRI rates above the epidemic threshold, which is defined as 1.50 cases per 100 trainees per week. (Figures 1, 2). The distribution of viral test results by site demonstrates the geographic variance in FRI etiology (Figure 3).

Temporal Trends – Epidemic level FRI rates peaked between February and April of 2001 at several sites, in contrast to historically described peaks during the winter months for FRI-like illnesses. This change in seasonal trends was also observed during the year 2000, as FRI rates above the epidemic threshold were observed during each month of that year.

FRI Specimens Tested per Site
June 1998 – April 2001

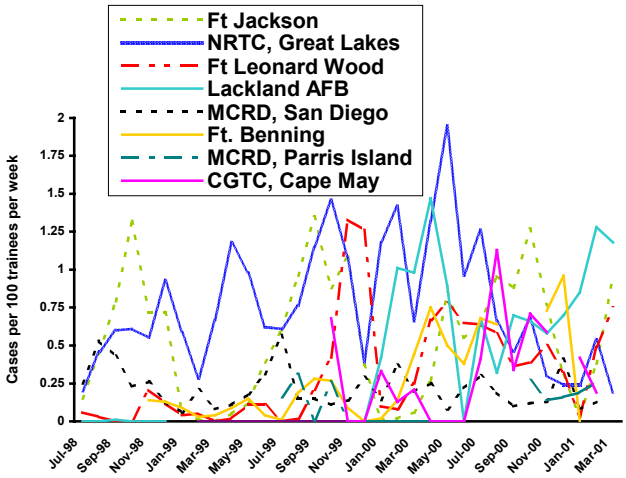
SITE	SPECIMENS TESTED
Fort Benning	989
Fort Jackson	2406
Fort Leonard Wood	1095
NRTC, Great Lakes	982
MCRD, San Diego	569
MCRD, Parris Island	264
CGTC Cape May	318
Lackland AFB	505

Adenovirus

Current Progress – In the absence of the vaccine, adenovirus remains the leading cause of febrile respiratory illness (FRI) among trainees. More than 60% of the 7191 throat cultures collected under the FRI study between June 1998 and April 2001 were positive for adenovirus. More than 96% of the adenovirus isolates collected to date have been type 4.

Geographic Trends – From January 1, 2001 to April 30, 2001, the amount of FRI morbidity caused by adenovirus continued to vary by location, ranging from 42.7% at Fort Leonard Wood, to 76.1% at MCRD San Diego. Please see accompanying chart for adenovirus infection rates by site.

Adenovirus Infection Rates at Basic Training Sites



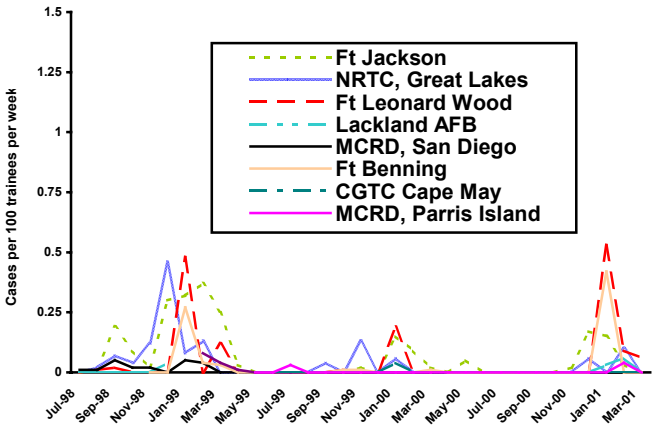
Influenza

Current Progress – From the start of this study in September 1998 to April 2001, 5.7% (408) of the 7191 FRI specimens tested thus far have been positive for influenza, with 4.2% identified as type A and 1.5% as type B. During this period, trainees who were not vaccinated against influenza were more than 4 1/2 times more likely to be influenza-positive (OR= 4.59, 95% CI, 3.64-5.80) than those who did receive the vaccine. During the most recent influenza season, from November 2000 to March 2001, 975 FRI specimens were tested. Of these, 8.5% (83) were identified as influenza, with type A comprising 4.1% of the total and 4.4% being type B. Surveillance data collected thus far indicate that influenza types A/New Caldonia/20199-like and B/Yamanashi/166-like were most prevalent during the 2000-2001 flu season.

Geographic Trends – Our surveillance data demonstrate that morbidity among trainees caused by infection with influenza A or B varies by training site location. During the 2000-2001 flu season, infection rates ranged from 0% at MCRD San Diego to 15.3% at Ft. Leonard Wood. Please see accompanying chart for influenza infection rates by basic training site location.

Temporal Trends – Influenza infection rates were highest at the recruit camps during the 1998-99 flu season, followed by high rates during the recent 2000-2001 flu season. In contrast, the 1999-2000 flu season demonstrated low infection rates as compared to the other two seasons surveyed.

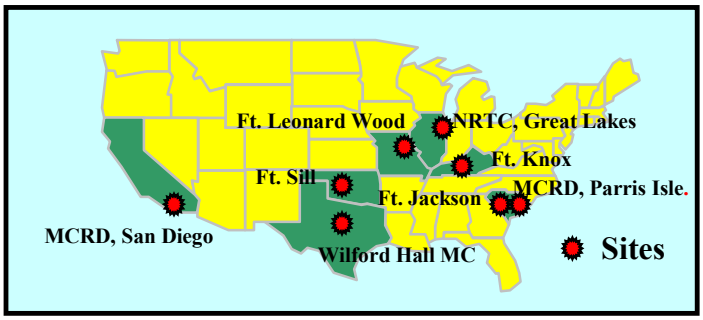
Influenza Infection Rates At Basic Training Sites



Other FRI Study Pathogens

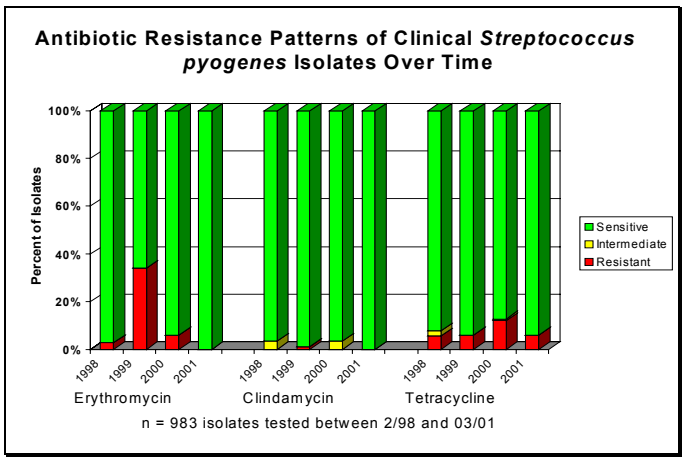
Of the 7191 throat cultures tested thus far under the FRI study, 21 (0.3%) have been positive for RSV and 73 (1.0%) have been positive for parainfluenza 1, 2, or 3.

Streptococcus pyogenes Surveillance



Current Progress – *Streptococcus pyogenes* (Group A streptococcus) continues to be a threat to the health of military trainees. Between February 1998 and March 2001, 406 clinical isolates were collected from trainees at 8 military sites.

Antibiotic Resistance – Among the specimens tested, *S. pyogenes* maintains 100% susceptibility to the antibiotics penicillin, levofloxacin, and vancomycin. Forty-one (10.1%) of the 406 isolates collected exhibited full or partial resistance to erythromycin, 37 (9.1%) to tetracycline, and 11 (3.0%) to clindamycin (Figure 4). Eight (2.0%) of the isolates were resistant to both erythromycin and tetracyline. Isolates from female trainees showed a similar proportion of erythromycin resistance as compared to male trainees (11.3% and 10.1%, respectively). Temporal trends in antibiotic resistance among *S. pyogenes* isolates collected to date demonstrate no discernible pattern, as shown in the following chart.



Emm-gene Types – As of April 2001, 144 *S. pyogenes* specimens had been emm-gene typed. Among these, the most common emm-gene types among military trainees were 6 (19.4%), 3 (13.2%), 2 (11.8%), 29 (9.7%), 12 (8.3%), and 75 (6.3). These seven emm-gene types made up more than 69% of all the typed isolates.

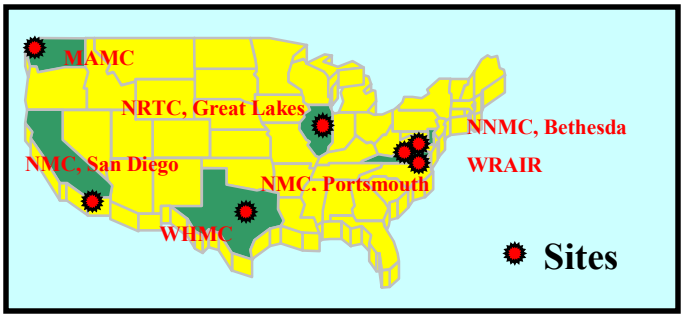
Resistance by Emm-gene type – Erythromycin resistance varied by emm-gene type. Type 75 exhibited the most erythromycin resistance of all emm-gene typed isolates, with 22% of type 75 isolates demonstrating full resistance.

Geographic Trends – *S. pyogenes* isolates from military trainees currently maintain high susceptibility to many commonly prescribed antibiotics, including penicillin, erythromycin and clindamycin. However, we continue to observe an unequal geographic distribution of erythromycin resistance at the sites. Resistance to erythromycin ranged from 0% at Fort Jackson and MCRD San Diego to 29.4% at Lackland AFB. Of the erythromycin resistant isolates from Lackland AFB, 100% were fully resistant.

S. pyogenes Isolates Received per Site
February 1998 – March 2001

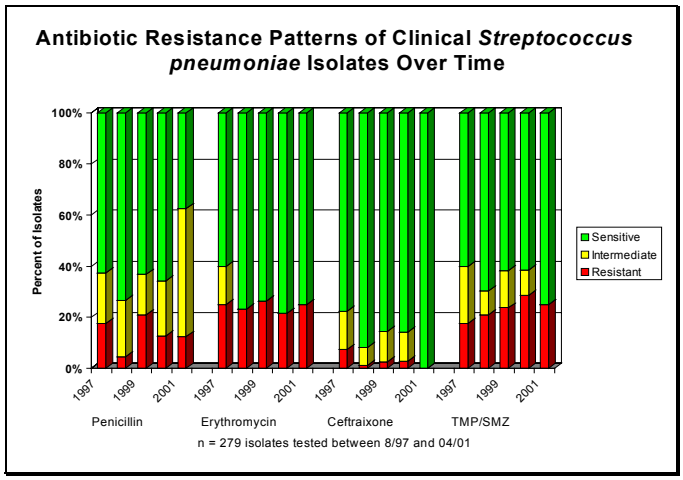
SITE	ISOLATES RECEIVED
NRTC, Great Lakes	89
MCRD, Parris Island	129
MCRD, San Diego	3
Fort Jackson	4
Fort Knox	23
Fort Leonard Wood	37
Fort Sill	19
Lackland, AFB	102

Invasive *Streptococcus pneumoniae* Surveillance



Current Progress – Testing is complete for 282 invasive clinical isolates collected between 8/97 and 04/01 from military healthcare beneficiaries at 7 military medical centers.

Antibiotic Resistance – Ninety-five (33.7%) of the 282 isolates collected demonstrated full or partial resistance to penicillin, and 63 isolates (22.3%) exhibited multiple resistance to three or more antibiotics (Figure 5). The resistance patterns between males (35.4% resistant) and females (31.4% resistant) were similar. Penicillin-resistance was observed across all age groups. The majority of penicillin isolates were obtained from individuals between two and sixty-five years of age, though the majority of isolates that were resistant to penicillin were found in individuals younger than one year of age or older than sixty-six years. As shown in the chart below, temporal trends in antibiotic resistance among *S. pneumoniae* isolates collected to date do not demonstrate a discernible pattern.



Geographic Trends – We observed an unequal geographic distribution of penicillin resistance among the collection sites. Penicillin resistance ranged from 0% at NRTC, Great Lakes to 50% at NMC Portsmouth. However, the number of isolates contributed by each site was not evenly distributed.

***S. pneumoniae* Serotypes** – Of the 142 typed isolates, the most common serotypes were 14 (23%), 6 (15%), 19

(15%), 9 (14%), 4 (11%), 23 (8%), and 18 (4%), all of which are included in the 23-valent pneumococcal vaccine. These seven serotypes made up more than 90% of the typed isolates at the sites.

Resistance by Serotype – Penicillin resistance differed by serotype, with types 19 (62.9%), 9 (60%), and 6 (45.5%) demonstrating the most resistance. These three serotypes accounted for more than 76% of all penicillin resistance among the serotyped isolates, though they only comprised 44% of the total number of serotyped isolates.

S. pneumoniae Isolates Received per Site August 1997 – April 2001

SITE	ISOLATES RECEIVED
NRTC Great Lakes	4
Naval Med. Ctr (NMC), San Diego	81
NMC, Portsmouth	2
National Naval Med. Ctr (NNMC), Bethesda	12
Walter Reed AIR	30
Wilford Hall MC	65
Madigan Army Med. Ctr. (AMC)	88

Bordetella pertussis Surveillance Study

Current Progress – Surveillance of *Bordetella pertussis* is currently underway at four military recruit training sites: MCRD-San Diego, Ft. Benning, Ft. Leonard Wood, and as of February 2001, at NRTC Great Lakes. To date, 162 specimens have been collected and tested using conventional culture methods. These specimens were collected from recruits meeting the case definition for pertussis, which is more than seven days of coughing as well as symptoms consistent with a respiratory infection. Preliminary results indicate that at least one (0.6%) of the specimens tested positive by culture techniques for the pathogen. Additionally, 35 specimens have been tested by PCR, and of those tested, 4 (11.4%) were positive for *B. pertussis*. Testing of sera specimens for evidence of pertussis infection is currently underway.

B. pertussis Isolates Received per Site June 2000 – April 2001

SITE	ISOLATES RECEIVED
MCRD San Diego	97
Fort Leonard Wood	47
Fort Benning	15
NRTC Great Lakes	3

Study Wrap Ups

Respiratory Syncytial Virus (RSV) Among Military Recruit Populations

This study, conducted at MCRD San Diego, Ft. Benning and HMS Raleigh in England, ended in June 2001. The goals of the study were to measure the proportion of FRI caused by RSV among recruits and to compare conventional culture methods with a new PCR diagnostic method. The final data analysis is currently underway.

Rapid Influenza Diagnostic Testing Quidel/BioStar

The evaluation of two rapid diagnostic influenza tests, Thermo-BioStar FluOIA® and Quidel QuickVue®, has been completed. The rapid tests are immunoassays that detect nucleoprotein antigens found in influenza A and B. These point-of-care tests provide results within 30 minutes, allowing for antiviral treatment of influenza-positive patients and reducing the inappropriate use of antibiotics. Recruits at Fort Benning, Fort Jackson, and Fort Leonard Wood with FRI symptoms were enrolled in the study, which was conducted during two time periods, from February through May 2000 and November 2000 through March 2001. Three nasal swabs were obtained from each recruit, one of which was used for each rapid test. The final swab was used for viral culture, which serves as the gold standard for viral detection. FluOIA testing was stopped for approximately four weeks in January 2001 and was resumed using throat swabs. The FluOIA and QuickVue tests had sensitivity of 100% (7/7) and 61% (30/49) respectively, and their specificity was 63% (243/384) and 93% (487/523). The FluOIA test performed poorly when throat swabs were used as the specimen type. It should be noted that both tests had claims of better performance when using other specimen types, however, those specimen types (such as naso-pharyngeal swabs) are more difficult to obtain and were deemed impractical in the recruit setting. Further study is needed to determine the optimal combination of specimen and test type in the recruit population.

New Proposals

Febrile respiratory illness (FRI) in a Mexican population – In collaboration with the Mexican Institute of Public Health Services, a one-year FRI surveillance project will begin in September or October of 2001 at a community clinic in Ensenada, Baja California, Mexico. The purpose of this pilot study is to determine the etiology of viral pathogens causing FRI among clinic attendees. A total of 200 throat swab specimens will be collected and tested using conventional viral culture

techniques. All clinic attendees who meet the case definition of FRI will be eligible for participation.

Association between adenovirus infections among military personnel and the development of obesity – This case control study, to begin later this year, will investigate if an association exists between weight control problems (obesity) and adenovirus-36 exposure in a population of active duty Navy personnel. The study will be conducted at the at the Clinical Trials Center in San Diego, with an enrollment goal of 300 individuals

Adenovirus serology – This study may use beginning- and end-of-training paired sera to measure the incidence of adenovirus infection during recruit training.

Room temperature specimens for PCR – This study may evaluate the performance of PCR tests in detecting adenovirus and influenza through the use of specimens that are stored at room temperature.

Shipboard FRI surveillance – NHRC may begin to monitor ships on deployment in a manner similar to the current FRI surveillance at basic training sites. This study may include viral culture testing and the calculation of FRI rates.

Restriction enzyme analysis of type 4 adenovirus – NHRC will examine the subtypes of adenovirus type 4 isolates accumulated over the past 5 years to look for geographic and/or temporal changes.

***S. pneumoniae* capsular typing** – Existing and future specimens from our *S. pneumoniae* surveillance will be serotyped to characterize geographic, temporal, and antibiotic resistance trends.

***S. pyogenes* emm typing** – Existing and future specimens from our *S. pyogenes* surveillance will be emm typed in order to characterize geographic, temporal, and antibiotic resistance trends.

Center News

Upcoming Conferences

- **Armed Forces Epidemiology Board**, September 18-19, Washington, D.C.
- **ICAAC**, September 22-25, Chicago, IL
- **50th Annual American Society of Tropical Med & Hygiene meeting**, November 11-15, Atlanta, GA

New Publications

- **Large epidemic of respiratory illness from adenovirus types 7 and 3 in healthy young adults.** Ryan M, Gray G, Smith B, McKeehan J, Hawksworth A, Malasig M. Clinical Infection Diseases, in press.
- **Report of two fatal cases of adenovirus-related illness in previously healthy young adults.** Ryan, M, et al. Morbidity and Mortality Weekly, Vol. 50 (26):553-5.
- **Handwashing and respiratory illness among young adults in military training.** Ryan MA, Christian RS, Wohlrabe. Am J Prev Med (Aug 2001); 21(2):79-83.
- **Simplified microneutralization test for serotyping adenovirus isolates.** Malasig MD, Goswami PR, Crawford-Miksza LK, Schnurr DP, Gray GC. J Clin Microbiology (Aug 2001); 39(8):2984-6.
- **National Department of Defense surveillance for invasive *Streptococcus pneumoniae*: Antibiotic resistance, serotype distribution, and arbitrarily primed polymerase chain reaction analyses.** Hudspeth MK, Smith TC, Barrozo CP, Hawksworth AW, Ryan MA, Gray GC. J Infect Dis (July 2001); 24:184(5).
- **B. pertussis detection by spectrofluorometry using polymerase chain reaction (PCR) and a molecular beacon probe.** Poddar SK, Le CT. Molecular and Cellular Probes (2001); 15:161-167.
- **Pneumococcal vaccine to counter emerging infectious disease threat in the military.** McKeehan J, et al. Military Medicine, in press.

Please contact the newsletter staff with any comments or suggestions regarding the information in this issue.

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These studies would not be possible without the hard work and dedication to excellence of the staff at our collaborating institutions.

Figure 1.

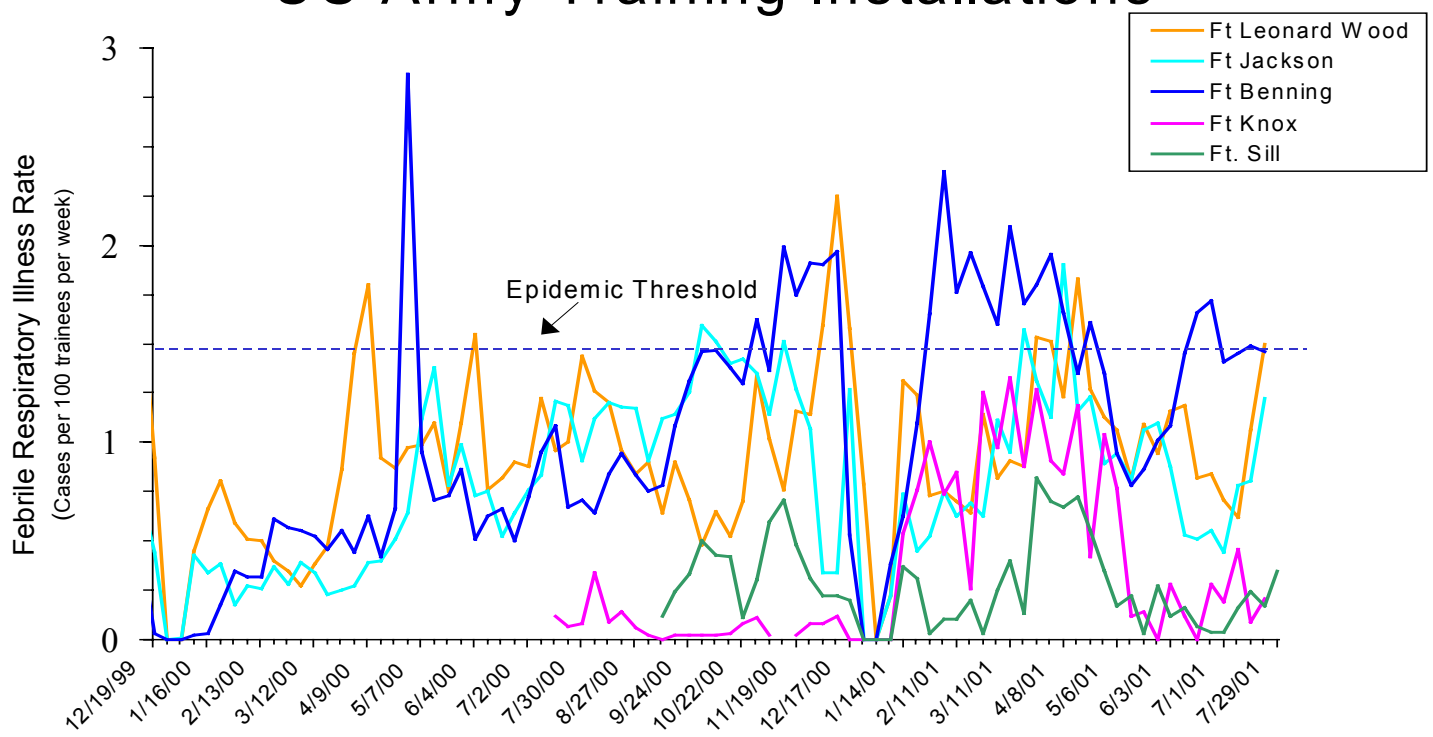


Figure 2.

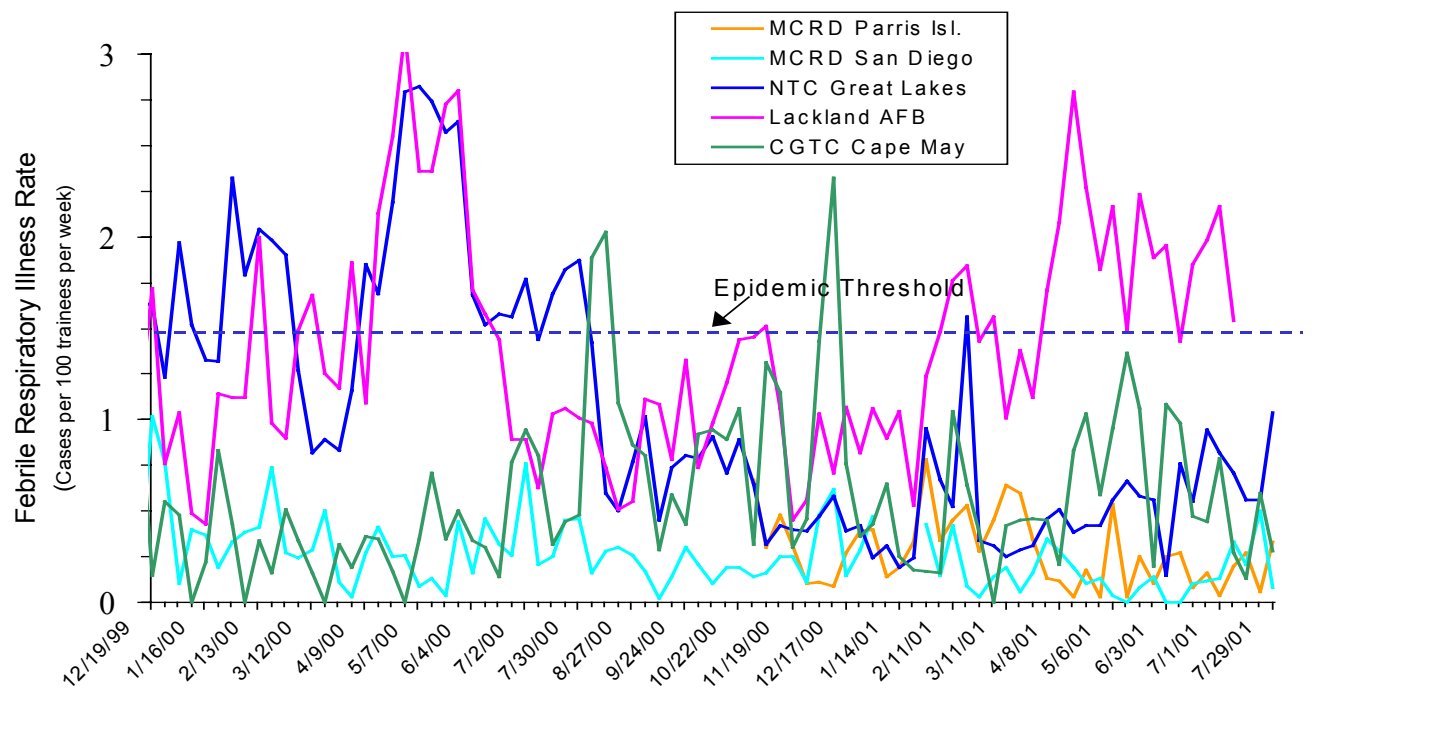


Figure 3.

Distribution of Viral Test Results by Site

June 1998 - April 2001
n=7191

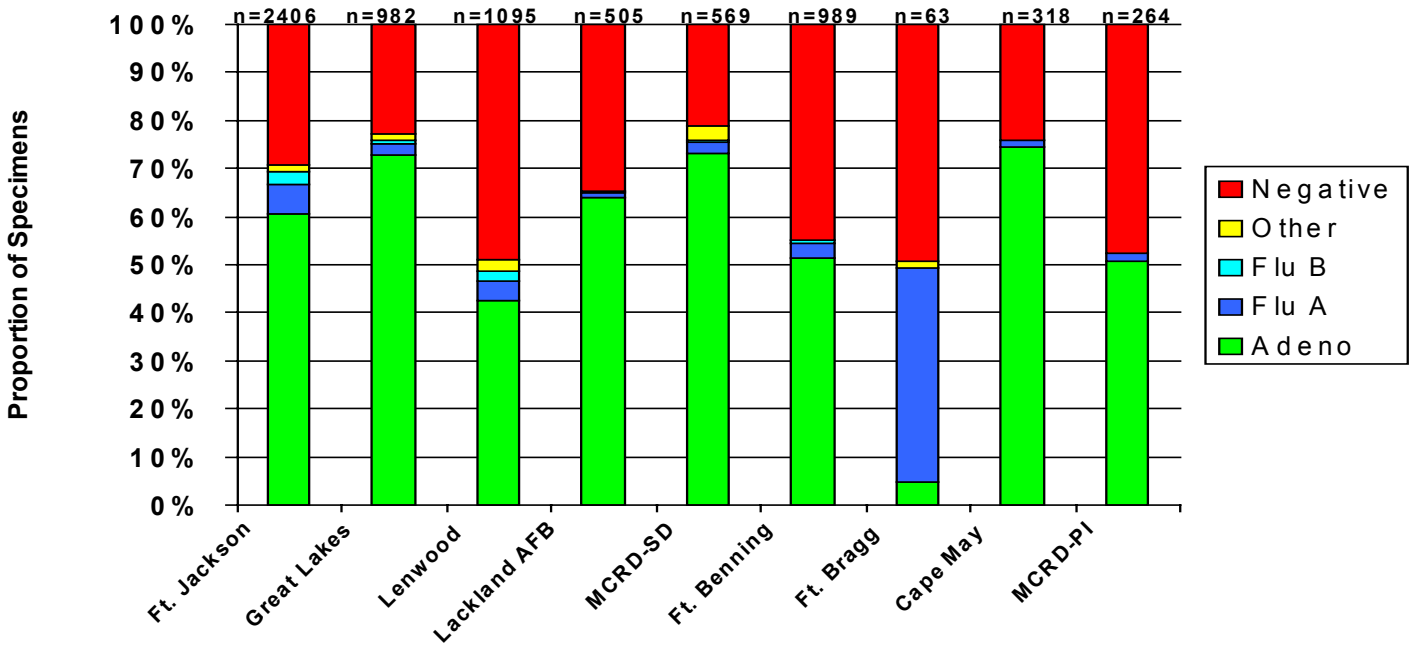
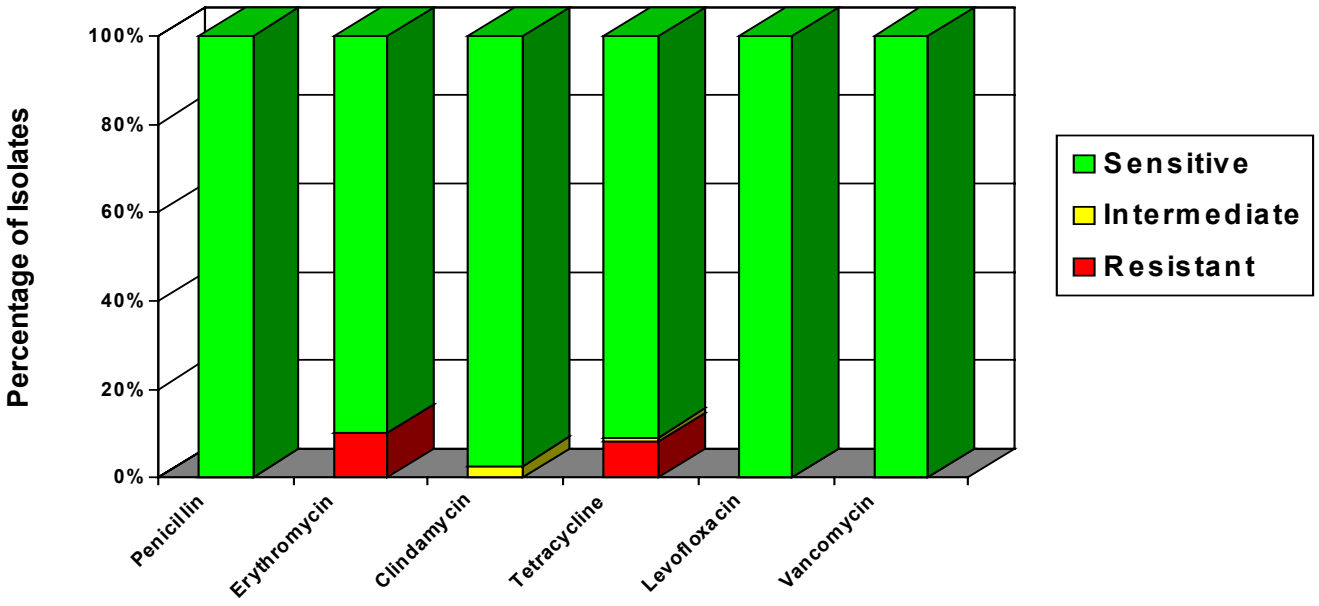


Figure 4.

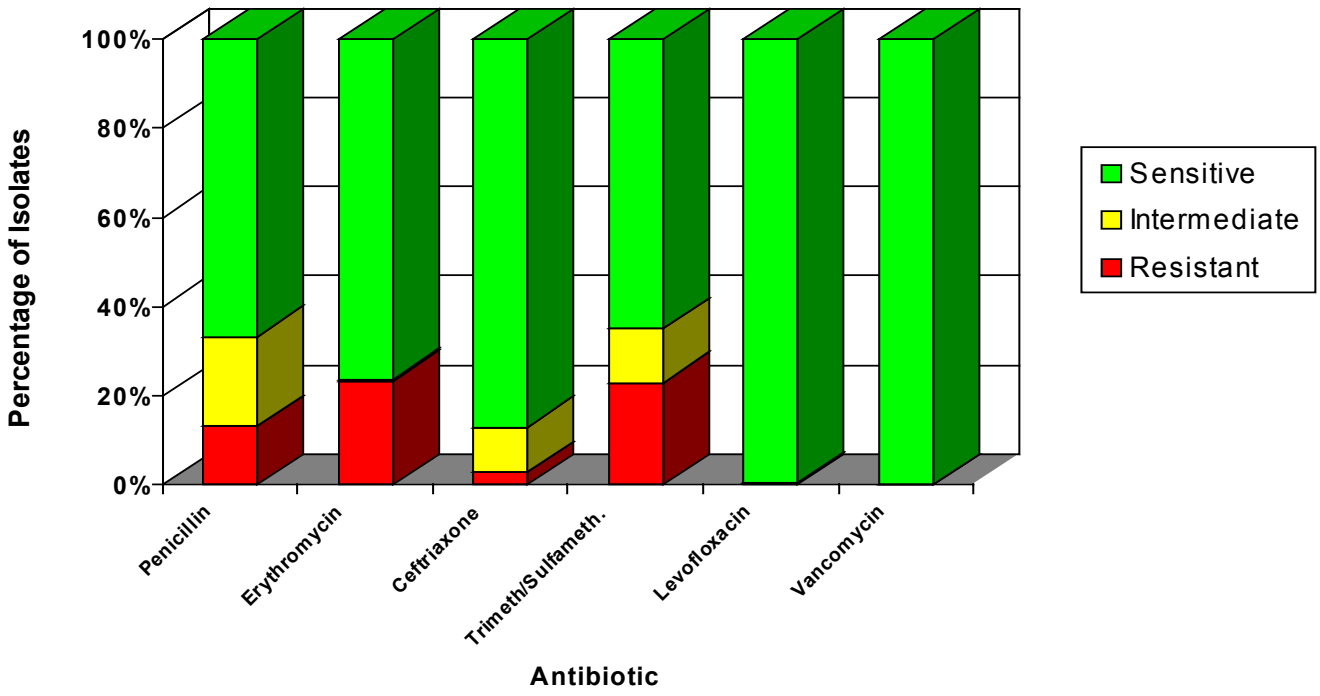
Antibiotic Resistance Patterns of Clinical *S.pyogenes* Isolates from Military Trainees



n=406 isolates tested between 2/98 and 03/01

Figure 5.

Antibiotic Resistance Patterns of Sterile Site *S. pneumoniae* Isolates From Military Medical Facilities



n=282 isolates tested between 8/97 and 04/01